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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/443,863	11/19/1999	INDU PARIKH	401930/SKYEPHARMA	7862

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EXAMINER	
KISHORE, GOLLAMUDI S	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/443,863	PARIKH ET AL.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-124* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The RCE filed on 12-16-04 is acknowledged.

Claims included in the prosecution are 50-124.

Claim Rejections - 35 USC § 103

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 50-124 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 98/07414 cited in the previous action. WO discloses the same process of preparation for the rapidly dispersing oral dosage forms of hydrophobic compounds wherein the particles are coated with at least two surfactants; one of the surfactants is a phospholipid (surface modifying agent). The average particle sizes of the hydrophobic compound are less than 10 microns. The composition contains other claimed materials such as celluloses and mannitol. The process of preparation involves the mixing of the components (water insoluble active agent and the surface modifying agents) in an aqueous medium, sonicating it and lyophilizing the composition to form particles (note the abstract, page 2, line 25 through page 8, line 19, Examples and claims). The process by WO differs from the claimed process in the amended claims in that, the bulking agent is added along with the active agent and the surface modifiers. However, in the paragraph bridging pages 7 and 8, WO teaches subjecting the mixture of the phospholipid and the active agent to procedures such as sonication and homogenization and the goes on to teach that mannitol and other agents may be added to adjust the

final formulation to isotonicity as well as a stabilizing agent during drying. It would have been obvious to one of ordinary skill in the art from these teachings that the addition of mannitol is a manipulatable parameter, that is, it can be added either before or after the homogenization step with the expectation of obtaining the best possible stabilized product. Instant invention therefore, is an obvious extension of the prior art's teachings. A careful review of instant specification on page 6 indicates that mannitol can be added prior to producing the micronized particles of the therapeutic agent (formulation) or to the homogeneous suspension of micro particles prior to freeze-drying and thus, this step does not appear to be critical.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that the claimed process surprisingly provides dried particles that are essentially devoid of
particle aggregation, even after reconstitution following periods of storage. This argument is not found to be persuasive since the prior art teaches the same composition and claims stability of the composition and control of particle growth. Since the same components will be present, one would expect the same properties upon the addition the addition of an aqueous medium and therefore, the examiner does not find that property surprising. Secondly, the claim are drawn to rapidly disintegrating dosage form which means they are for oral administration and disintegrate either in the mouth and in acidic stomach and applicant has not shown that the prior art form and instant form have different properties under these conditions. Finally it should be pointed out that instant

claims do not recite any amounts for the components other than phospholipids. For this reason applicant's arguments that mannitol in the prior art is added only to adjust the isotonicity are not found to be persuasive. As applicants themselves admit, mannitol is added in the prior art also as a stabilizing aid.

3. Claims 50-124 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yarwood (5,827,541) in further combination with Green (5,976,577) of record or Na (5,326,552) or WO 98/07414 cited above by themselves or in combination.

Yarwood discloses a process for the rapidly dispersing oral dosage forms of hydrophobic compounds wherein the particles are coated with a surfactant (surface modifying agent). The surfactant taught is claimed poloxamer. The average particle sizes of the hydrophobic compound are less than 10 microns. The composition contains other materials such as celluloses and mannitol. The process of preparation involves the mixing of the components and lyophilizing the composition to form particles. (note the abstract, column 1, line 54 through col. 4, line 14, Examples and claims). Yarwood does not disclose phospholipids as the surfactant; Yarwood also does not teach a combination of surfactants. However, it should be pointed out that according to Yarwood on col. 2, line 51 et seq., any surfactant, which fulfills the requirement of pharmaceutical acceptability, may be used. Therefore, it would have been obvious to one of ordinary skill in the art to use phospholipids which are well know surfactants in the process of Yarwood based on this suggestion and from the guidance provided with a reasonable expectation of success.

One of ordinary skill in the art would be further motivated to use phospholipids with the expectation of obtaining at least similar results, in view of the references of Green, and Na and WO all of which teach the use of phospholipids to coat sub-micron size particles just as in instant method (see abstract and col. 5, lines 30-48 of Green; abstract, col. 2, lines 49-53; col. 3, line 65 through col. 4, line 38 of Na). What is also lacking in Yarwood is the teaching of the addition of mannitol as a separate step. However, since Yarwood is directed to rapidly dispersing oral dosage form same as in instant method, it is deemed obvious to one of ordinary skill in the art to manipulate the basic method of Yarwood with the expectation of obtaining the best possible results. Furthermore, as pointed out above, in the paragraph bridging pages 7 and 8, WO teaches subjecting the mixture of the phospholipid and the active agent to procedures such as sonication and homogenization and the goes on to teach that mannitol and other agents may be added to adjust the final formulation to isotonicity as well as a stabilizing agent during drying. It would have been obvious to one of ordinary skill in the art from these teachings that the addition of mannitol is a manipulatable parameter, that is, it can be added either before or after the homogenization step with the expectation of obtaining the best possible stabilized product. Instant invention therefore, is an obvious extension of the prior art's teachings. A careful review of instant specification on page 6 indicates that mannitol can be added prior to producing the micronized particles of the therapeutic agent (formulation) or to the homogeneous suspension of micro particles prior to freeze-drying and thus, this step does not appear to be critical.

NOTE: upon consideration, the rejection of claims on Yarwood alone is withdrawn.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Yarwood does not include a phospholipid in combination with an active agent, one or more surface stabilizing agents and one or more bulking/releasing agent. The examiner disagrees with applicants' characterization of Yarwood's composition as lacking active agent and bulking agent since Yarwood teaches mannitol (col. 5, line 5) and Yarwood clearly teaches that the formulation is for hydrophobic active agents. With regard to lack of teachings of phospholipid in Yarwood, the examiner points out that the secondary references teach the use of phospholipids and Na in particular teaches that phospholipids are surface modifiers. Applicant argues that Yarwood teaches gelatin as the carrier material. This argument is not found to be persuasive since instant claims do not exclude gelatin.

Applicant's arguments with regard to Green are not found to be persuasive. Applicant argues that Green teaches that phospholipids are among many types of polymer or lipid material, which may be used to coat the particles. This argument is not persuasive since Green is suggestive of the use of phospholipids as a coating material as applicants themselves recognize. Applicants' arguments that Green teaches away because he advocates larger particles are not found to be persuasive since the reason for such is to prevent the rapid release in the mouth itself. The use of smaller sizes is implicit from this teaching if one wants a rapid release in the stomach instead of mouth. This is not teaching away.

Applicants' arguments based on the declaration of Misra that Green's teachings would result in agglomerated particles are not persuasive since Green is combined for the teachings of phospholipids and the references of Na and WO which are used in the rejection show no such agglomeration. Applicants' arguments that NA teaches diagnostic compounds and that the particle sizes in Na are less than 400 nm are not found to be persuasive since Na is combined to show that phospholipids are commonly used surfactants to coat nanoparticles. Furthermore, on col. 3, lines 33-45 Na teaches that course particles can be reduced in size using conventional milling method and therefore, one of ordinary skill in the art would be motivated to prepare particles of desired sizes. The examiner has already addressed applicants' arguments with regard to WO.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 50-124 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 5,922,355. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. Claims in the said patent are drawn to a process of preparing microparticles of water insoluble drugs mixing the drug, a phospholipid and another surfactant and applying energy to reduce the particle sizes. Although patented claims do not specifically recite adding the bulking materials such as mannitol, the claims recite 'comprising the steps of' and that applicants's intent to include bulking material such as mannitol in the comprising language is clear from the examples in the said patent which steps are claimed in instant claims. Instant steps of adding the bulking materials thus, is deemed to be included in the patented method claims.

6. Claims 50-124 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,228,399. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. Claims in the said patent are drawn to a process of preparing microparticles of water insoluble drug, cyclosporin by mixing the drug, a phospholipid and another surfactant and applying energy to reduce the particle sizes. Although patented claims do not specifically recite adding the bulking materials such as mannitol, the claims recite 'comprising the steps of' and that applicants's intent to include bulking material such as mannitol in the comprising language is clear from the examples in the said patent which steps are claimed in instant claims. Instant

steps of adding the bulking materials thus, is deemed to be included in the patented method claims. Instant generic term, water insoluble drug includes cyclosporine in the patented claims.

7. Claims 50-124 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 6,465,016u. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. Claims in the said patent are drawn to a process of preparing microparticles of water insoluble drug, cyclosporin by mixing the drug, a phospholipid and another surfactant and applying energy to reduce the particle sizes. Although patented claims do not specifically recite adding the bulking materials such as mannitol, the claims recite 'comprising the steps of' and that applicants's intent to include bulking material such as mannitol in the comprising language is clear from the examples in the said patent which steps are claimed in instant claims. Instant steps of adding the bulking materials thus, is deemed to be included in the patented method claims. Instant generic term, water insoluble drug includes cyclosporine in the patented claims.

8. Claims 50-124 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-44 of copending Application No. 10/443,772. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent

granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: the claims in the copending application are drawn to fenofibrate compositions and a process of preparation of those compositions involving the same steps as in instant application. Instant generic 'water insoluble drug' is deemed to include fenofibrate in the claims of said copending application.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

9. Claims 50-124 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2, 4-25, 45-47, 52-53, 55-56, 65 and 101-119 of copending Application No. 10/260,788 Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the copending application are drawn to the same process of preparation and the products resulting from said process and the process is directed to water insoluble drugs. Although the independent claims in said copending application do not recite the addition of bulking materials such as mannitol, the language, 'comprises' provides for the inclusion of such step. Furthermore, the dependent claim 115 in fact recites mannitol. It is obvious therefore, that such a step is included as in instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM-4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK